Efficacy and safety of cagrilintide s.c. 2.4 mg in combination with semaglutide s.c. 2.4 mg (CagriSema s.c. 2.4 mg/2.4 mg) once-weekly in participants with overweight or obesity

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This study has been transitioned to CTIS with ID 2023-506929-11-00 check the CTIS register for the current data. Primary To confirm superiority on body weight reduction of CagriSema 2.4 mg/2.4 mg versus placebo as adjuncts to reduced-calorie diet...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53435

Source
ToetsingOnline

Brief title
NN9838-4608

Condition

- Other condition

Synonym
Obesity, overweight

Health condition

obesitas en overgewicht

Research involving
Human

Sponsors and support

Primary sponsor: Novo Nordisk
Source(s) of monetary or material Support: Novo Nordisk

Intervention

Keyword: cagrilintide, once-weekly, overweight or obesity, semaglutide

Outcome measures

Primary outcome

Relative change in body weight From baseline (week 0) to end of treatment (week 68) %

Achievement of >= 5% weight reduction From baseline (week 0) to end of treatment (week 68)

Secondary outcome

Achievement of >= 20% weight reduction From baseline (week 0) to end of treatment (week 68)

To confirm superiority of CagriSema 2.4 mg/2.4 mg versus placebo on achievement of >= 25% weight reduction.

Achievement of >= 25% weight reduction From baseline (week 0) to end of treatment (week 68)

To confirm superiority of CagriSema 2.4 mg/2.4 mg versus placebo on achievement of >= 30% weight reduction.

Achievement of >= 30% weight reduction From baseline (week 0) to end of treatment (week 68)

To confirm superiority of CagriSema 2.4 mg/2.4 mg versus cagrilintide 2.4 mg on body weight.

To confirm superiority of CagriSema 2.4 mg/2.4 mg versus semaglutide 2.4 mg on body weight.

Relative change in body weight From baseline (week 0) to end of treatment (week 68) %

To confirm superiority of CagriSema 0.5 mg/0.5 mg versus placebo on body weight

Relative change in body weight From baseline (week 0) to week 8 %

To confirm superiority of CagriSema 2.4 mg/2.4 mg versus placebo on body weight

Relative change in body weight From baseline (week 0) to week 20 %

To confirm superiority of CagriSema 2.4 mg/2.4 mg versus placebo on:

• Waist circumference

• Systolic blood pressure

• Physical functioning Change in waist circumference From baseline (week 0) to end of treatment (week 68) cm

Change in systolic blood pressure (SBP) From baseline (week 0) to end of treatment (week 68) mmHg

Change in Impact of Weight on Quality Of Life-Lite Clinical Trials Version (IWQOL-Lite-CT) Physical Function score From baseline (week 0) to end of treatment (week 68) Score points

Change in Short Form-36 Version 2.0 (SF-36v2) Physical Functioning score From baseline (week 0) to end of treatment (week 68) Score points

Secondary supportive safety endpoints

To compare the safety and tolerability of CagriSema 2.4 mg/2.4 mg versus

placebo, semaglutide 2.4 mg and cagrilintide 2.4 mg.

Number of Treatment-emergent Adverse Events (TEAEs) From baseline (week 0) to

end of studymain (week 75) Count of events

Number of Treatment-emergent Serious adverse events (TESAEs) From baseline

(week 0) to end of studymain (week 75) Count of events

Study description

Background summary

The prevalence of obesity has been increasing during the last 30 years and globally, more than
650 million people have obesity. Obesity is associated with an increased risk of developing type 2
diabetes (T2D), dyslipidaemia, hypertension, cardiovascular (CV) disease, obstructive sleep
apnoea, Non-Alcoholic Fatty Liver Disease/Non-Alcoholic Steatohepatitis (NAFLD/NASH),
urinary incontinence, several types of cancers, and increased mortality. In addition,
individuals with obesity experience reduced health-related quality of life including reduced physical
function. Several associations, organisations and individual countries have recognized that
obesity should be treated as a chronic disease.

Semaglutide is a Glucagon-Like Peptide-1 (GLP-1). GLP-1 is an incretin hormone released from intestinal L-cells with a glucose-dependent stimulatory effect on insulin and inhibitory effect on glucagon secretion from the pancreatic islets. In addition, supraphysiological levels of GLP-1 induce reduction in body weight.

Cagrilintide is an amylin analogue. Endogenous amylin is a neuroendocrine peptide hormone that is co-secreted with insulin by pancreatic beta-cells in response to food intake. It affects a number of GI processes including delay of gastric emptying and suppression of post-prandial glucagon release.

Cagrilintide in combination with semaglutide is currently under development by Novo Nordisk for the weight management indication. Combining anti-obesity medications with different modes of action may offer superior weight loss when compared to the monocomponents.

Study objective

This study has been transitioned to CTIS with ID 2023-506929-11-00 check the CTIS register for the current data.

Primary
To confirm superiority on body weight reduction of CagriSema 2.4 mg/2.4 mg versus placebo as adjuncts to reduced-calorie diet and increased physical activity in participants with overweight or obesity.

Secondary
To confirm superiority of CagriSema 2.4 mg/2.4 mg versus placebo on achievement of >= 20% weight reduction.

Study design

The study consists of a main phase and an extension phase.
The total duration of the main phase for each participant will be approximately 78 weeks (up to 3 weeks screening, 68 weeks treatment and 7 weeks follow-up).
The 68-week main phase of the present study is designed to compare the efficacy and safety of once-weekly cagrilintide s.c. in combination with semaglutide s.c. (CagriSema s.c.) versus once-weekly cagrilintide s.c., semaglutide s.c. and s.c placebo, all as an adjunct to a reduced-calorie diet and increased physical activity, for weight management in participants with overweight or obesity.
After the main phase there will be a waiting period for all randomised participants until DBL and unblinding of sponsor has occurred. After the waiting period the participants will be informed if they are in the extension phase or not. Only participants randomised to either CagriSema or placebo are part of the extension phase. During the extension phase, participants will not receive study intervention (i.e. neither intervention with diet and physical activity counselling nor investigational medicinal product (IMP)) and will thus be considered off-treatment.
The duration of the extension phase, including the waiting period, is 97 weeks.

Intervention

Subjects are randomised (21:3:3:7) in the groups: subcutaneous injection of cagrisema (cagrilintide/semaglutide) 2.4 mg/2.4 mg, cagrilintide 2.4 mg, semaglutide 2.4 mg or placebo once weekly.
All participants will receive counselling on diet and physical activity,

provided by a dietitian or similar qualified health professional, every 4th week at the remote/site visits during the treatment period and at end of studymain visit (V26).

Study burden and risks

Participants will be treated with a regimen anticipated to be better than or equal to the weight management they receive at the time of entry into the study. In the semaglutide weight management programme, the 68-week STEP 1 study (NN9536-4373), which included a similar study population as this study, demonstrated clinically significant weight loss with semaglutide s.c. 2.4 mg once-weekly.
Semaglutide s.c. 2.4 mg once-weekly had a safe and well-tolerated profile, consistent with previous findings for semaglutide and GLP-1 RAs.
A 26-week phase 2 clinical study (NN9838-4433) investigating cagrilintide once-weekly has been completed in participants with overweight or obesity. A dose dependent decrease in body weight with increasing doses of cagrilintide was demonstrated. A higher proportion of participants achieved a body weight loss of at least 5% and 10% at week 26 with increasing doses of cagrilintide compared to participants that received placebo.
A 20-week treatment phase 1 clinical study (NN9838-4395) investigating ascending once-weekly doses of cagrilintide in combination with semaglutide has been completed in participants with overweight or obesity. A substantial weight loss was observed in participants receiving cagrilintide 1.2, 2.4, and 4.5 mg in combination with semaglutide 2.4 mg when compared to placebo with semaglutide 2.4 mg.
In addition, it is expected that all participants will benefit from participation through close contact with the site staff and diet and physical activity counselling by a dietician or a similar qualified healthcare professional.
Extension phase
Participants who continue in the extension phase are expected to benefit from the continued contact with the site staff focusing on general health, including body weight, CV risk factors and glucose metabolism parameters.

Taking into account the measures taken to minimise risk and burden to participants participating in this study, the potential risks identified in association with CagriSema, cagrilintide and semaglutide are justified by the anticipated benefits that may be afforded to participants with overweight or obesity.

Contacts

Public

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male or female
- Age above or equal to 18 years at the time of signing informed consent
- BMI greater than or equal to 30.0 kg/m^2 or b) BMI greater than or equal to 27.0 kg/m^2 with the presence of at least one weight related comorbidity including, but not limited to hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease

Exclusion criteria

Glycaemia related:
-HbA1c greater than or equal to 6.5 % (48 mmol/mol) as measured by the central laboratory at screening
-History of type 1 or type 2 diabetes mellitus

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-01-2023
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	cagrilintide
Product type:	Medicine
Brand name:	Wegovy
Generic name:	semaglutide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	01-06-2022
Application type:	First submission
Review commission:	METC NedMec

Approved WMO Date:	13-10-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	26-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-04-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-06-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-06-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-06-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	19-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-11-2023
Application type:	Amendment
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-506929-11-00
EudraCT	EUCTR2020-005435-75-NL
CCMO	NL80969.041.22